As already mentioned, once the defect is secured, it may be transmitted to subsequent generations through breeding. So far we have succeeded in passing it to the sixth generation. There seems to be no reason why it will not go on indefinitely since the imperfection tends to become worse in succeeding generations and also to occur in a proportionally greater number of young. The transmission was not infrequently of an irregular unilateral type, sometimes only the right, at others only the left eye showing the defect. In later generations there was an increasing number of young which had both eyes affected.

To meet the objection that we were not getting instances of true inheritance in each generation but merely placental transmissions of antibodies or kindred substances from the blood stream of the mother, it was obviously necessary to establish the descent through the male line alone. To do this females from strains of rabbits unrelated to our defective-eyed stock were mated to defective-eyed males. The first generation produced in this way were invariably normal-eyed, but when females of this generation in turn were mated to defective-eyed males the defect reappeared in some of the progeny somewhat after the manner of an extracted Mendelian recessive. Inasmuch as the defect can thus be made to reappear in the descendants of a male with abnormal eyes when he is mated to a female from unrelated and untreated stock, it is obvious that it could only have been conveyed through the germ-cells of the male, and that it may, therefore, be pronounced an example of true inheritance.

The detailed study, with charts, pedigrees, drawings and photographs will appear shortly in the *Journal of Experimental Zoölogy*.

ON THE MECHANISM OF FEVER REDUCTION BY DRUGS

By Henry G. Barbour and Julian B. Herrmann

Department of Pharmacology, Yale University, School of Medicine

Communicated by L. B. Mendel, Read before the Academy, November 10, 1919

Correlation of antipyretic drug action with the carbohydrate metabolism has been suggested by one of us[1] as a result of two findings in fever patients. In the first place dextrose by mouth has been found frequently to exert a mild antipyretic action; on the other hand, acetyl-salicylic acid or antipyrine under similar conditions increase the respiratory quotient, thus indicating a relatively augmented carbohydrate combustion. These facts point strongly to a mobilization of sugar by such drugs.

We have, therefore, investigated the effects of antipyretics upon normal and fevered dogs with particular attention to the concentration of dextrose in the blood. Mild fever was produced by the subcutaneous injection upon the preceding day of a suspension of killed colon bacilli. Doses of from 0.2 to 0.5 gram. per kilo of the following drugs were given: sodium salicylate, quinine hydrochloride, antipyrine (all subcutaneously)

and acetyl-salicylic acid (per os). In fevered dogs a fall in body temperature of about 1° C. resulted; on the other hand a slight increase was the only observed change in the temperature of normal animals.

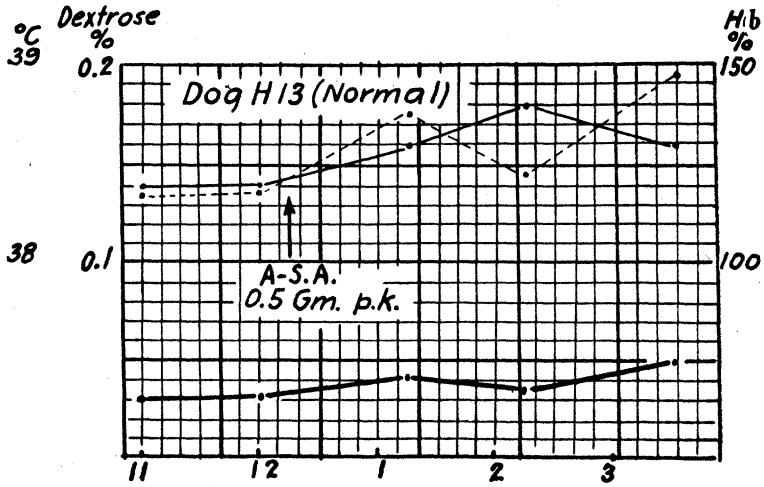

FIG. 1. Effects of acetyl-salicylic acid (0.5 gm. per kilo) on normal dog. Rectal temperature: light line; blood dextrose per cent: broken line; hemoglobin per cent: heavy line.

Blood Dextrose.—Both series of dogs were subjected to investigation of the blood sugar concentration by the Benedict-Lewis method. In all animals irrespective of the fevered condition there resulted a moderate hyperglycaemia, the extent of which may be judged from the following summary:

DEXTROSE CONCENTRATION IN THE BLOOD

	BEFORE ANTIPYRETIC %	MAXIMUM AFTER ANTIPYRETIC %
Average of 13 normal dogs	0.137	0.186
Average of 10 fevered dogs	0.139	0.218

Blood Volume.—The hemoglobin concentration was followed in most of these experiments simultaneously with the blood sugar, employing the colorimetric method of Cohen and Smith.[2] In the normal dogs was found a rise in the hemoglobin percentage accompanying the slight temperature increase. The thickening of the blood thus indicated was insignificant in comparison with the observed dextrose increase, the latter being thus proven absolute rather than merely relative.

Fevered dogs, on the other hand, showed a distinctly increased blood volume as indicated by the diminished hemoglobin percentage accompanying the antipyretic effect. Dilution of the blood of fever patients by acetyl-salicylic acid and by antipyrine has also been observed by one of us.

The above described effects as exemplified in normal and fevered dogs are illustrated in figures I and II, respectively. The following conclusions have been drawn from this work:

(1) A variety of antipyretic drugs increase the blood sugar in both normal and fevered dogs.

(2) In the latter this effect is accompanied by a dilution of the blood (indicated by diminished hemoglobin percentage) and a fall in temperature, neither of which occur in healthy animals.

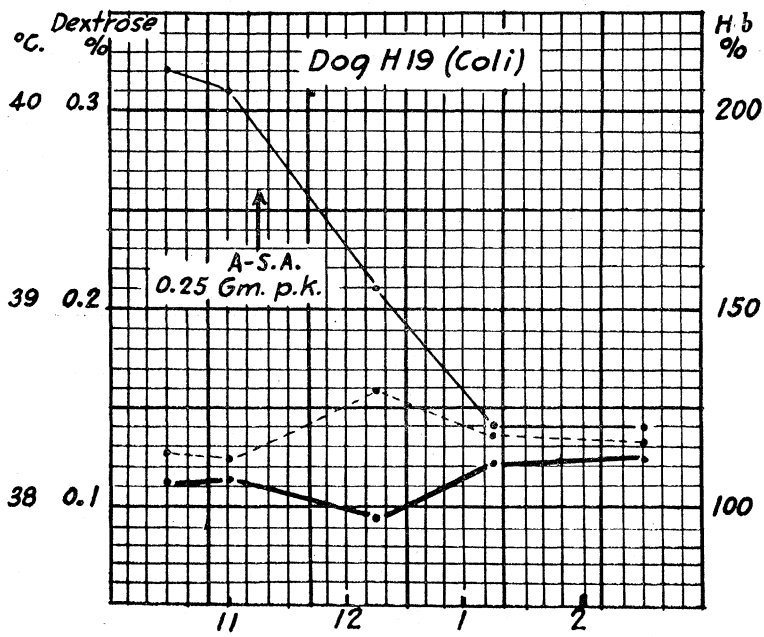

FIG. 2. Effects of acetyl-salicylic acid (0.25 gm. per kilo) on dog treated on preceding day with suspension of killed colon bacilli. (See Fig. 1.)

(3) *Theory of the mechanism of fever reduction by drugs.*—Antipyretic drugs increase the blood content of dextrose, a substance itself often exhibiting temperature-reducing properties when introduced from without. Moderate hyperglycaemia favors dilution of the blood.[3] In fevered animals antipyretics actually produce such a plethora, the hyperglycaemia probably contributing largely to this effect. Plethora promotes dissipation of heat both by radiation (peripheral vaso-dilation) and water evaporation from the surface of the body. The occurrence of plethora with its resulting anti-pyretic effect is apparently limited to fevered animals. This fact should probably be attributed not so much to a greater degree of hyperglycaemia as to the relative water retention by the tissues which is said to accompany febrile conditions.[4]

[1] Barbour, H. G., "Antipyretics" (Papers I and III), *Arch. Int. Med.*, Dec., 1919; and *Proc. Soc. Exp. Biol. Med.*, **16**, 1919 (136).

[2] Cohen, B. and Smith, A. H., *J. Biol. Chem.*, **39**, 1919 (489).

[3] Cf. Fisher, G. and Wishart, M. B., *J. Biol. Chem.*, **13**, 1912 (49).

[4] A part of the expenses of the work herein reported has been defrayed from the Francis E. Loomis Research Fund of the Yale University School of Medicine. More extensive reports will be sent to the *Journal of Pharmacology & Experimental Therapeutics* and to the *Archives of Internal Medicine*.

INFERENCES FROM THE HYPOTHESIS OF DUAL ELECTRIC CONDUCTION; THE THOMSON EFFECT

BY EDWIN H. HALL

JEFFERSON PHYSICAL LABORATORY, HARVARD UNIVERSITY

Communicated January 29, 1920

At the Washington meeting of the National Academy of Sciences in April, 1919, I presented two papers that have not yet been published. One was on the *Effect of Pressure on Electric Resistance and on Peltier Heat in Metals*, the other on *Thermal Conduction in Metals*, both being written from the standpoint of Dual Electric Conduction.

The first named of these two papers contained implicitly the following propositions:

1*a*. Increase of pressure should, by bringing the atoms and the metal ions closer together, increase k_a, the associated-electron conductivity, and decrease k_f, the free-electron conductivity. We might, then, expect the total conductivity, k, to increase under pressure in metals having a relatively small value of $(k_f \div k_a)$ and to decrease in metals having a relatively large value of this ratio.

1*b*. As antimony and bismuth have exceptionally small values of k, they probably have exceptionally large values of $(k_f \div k_a)$, and this may account for the fact that, among twenty metals examined by Bridgman, these two were the only ones to show a decrease of conductivity under an increase of pressure.

2*a*. If the ratio $(k_f \div k_a)$ is greater in metal B than in metal A, ionization must occur at the junction of the two metals when a current flows from A to B, and re-association must occur there when the current flows from B to A. As ionization is doubtless accompanied by absorption of heat and re-association by evolution of heat, we have here an action which may play a very important part, if not the chief part, in the Peltier effect.

2*b*. The exceptionally large value of $(k_f \div k_a)$ that probably exists in bismuth may account for the fact that heat is absorbed when a negative current goes into this metal from any other.

2*c*. As increase of pressure probably decreases the ratio $(k_f \div k_a)$, we should expect an absorption of heat where a negative current flows from a metal under high pressure to the same metal uncompressed. If we call this effect of compression *plus* and the opposite effect *minus*, we